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ON LYMPH PRODUCTION. By E. H. STARLING,
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THE INFLUENCE OF MECHANICAL FACTORS ON
LYMPH PRODUCTION. BY ERNEST H. STARLING,
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UNTIL recently, the prevailing opinion of physiologists respecting the formation of lymph was that it was, to a large extent at any rate, a process of filtration, and that the lymph-flow was determined by differences of pressure and composition between the blood in the vessels and the fluids filling the interstices of the tissues. Ludwig² in his Textbook speaks of the lymph-flow as being conditioned by two factors,—firstly differences in the pressure of the blood in the capillaries and the fluid in the tissue spaces giving rise to an exudation of fluid through the capillary walls, and secondly chemical differences between these two fluids setting up osmotic interchanges through the blood-vessel wall. This, the mechanical theory of lymph production, has been the guiding idea in the researches on the subject which have been carried out in Ludwig's laboratory. These chiefly considered the effects of changes in the pressures obtaining in and outside the vessels on the lymph-flow. If the lymph is produced by a simple act of filtration through the passive capillary walls, then the amount of lymph produced must rise and sink with the value of $D - d$, where D represents the blood-pressure inside the capillaries, and d the pressure of the lymph in the tissue spaces with which the capillaries are surrounded.

The results of the investigation of the lymph-flow from various regions have however only afforded a partial confirmation of this theory. It is true that increased capillary pressure in consequence of venous obstruction (Tomsa, Emminghaus) increases the flow of lymph.

¹ The paper (p. 159) on venous pressures, by Bayliss and myself, should be read before this paper, since the results there obtained form the basis of the main argument used in the following pages.

² Ludwig. *Lehrbuch der Physiologie*. Bd. II. S. 562 (Zweite Auflage, 1861).

The transudation is moreover increased when the pressure in the lymph spaces is diminished by squeezing out the lymph previously contained in them. It is only by employing this latter method that any lymph at all can be obtained from a dog's limbs at rest. On the other hand the investigations carried out in the Leipzig laboratory failed to establish any connection between capillary pressure and lymph-flow, when the former was increased by changes in the arterial pressure. Thus Paschutin¹, working on the lymph production from the whole fore limbs, found that the active hyperaemia caused by section of the brachial plexus and stimulation of the cord brought about no increase in the lymph-flow.

Emminghaus², carrying out similar experiments on the hind paw of dogs, failed in most experiments to get any increase in lymph-flow in consequence of an active hyperaemia. In only two experiments did he obtain a slight increase of the lymph which could be squeezed out of the foot, after section of the sciatic nerve.

Later on Rogowicz³ reinvestigated the question under Heidenhain's guidance, and found that an active hyperaemia did have some effect in increasing the lymph production in the paw. The absolute effect was however small in comparison with that produced by venous obstruction.

The very small effect on lymph production which is produced by considerable changes in the blood-flow to the capillaries, and in the arterial pressure, throws considerable difficulties in the way of regarding the process of lymph formation simply as one of filtration, and Paschutin himself, in acknowledging the difficulty, suggests the possibility of another factor, such as changes in the capillary wall itself, being involved.

The existence of such a factor is shown further by the action of curare. It was pointed out by Paschutin and later on by Rogowicz that curare appears to exert a specific influence on lymph formation in the limbs, quite independently of any effect it might have on the blood-pressure, and the latter author suggests that there may be substances, which have a specific action increasing the lymph-flow just as diuretics increase the urinary secretion. This paper was published in 1885. In the same year Tigerstedt and Santesson⁴ discuss the question of

¹ *Ludwig's Arbeiten*, 1873, p. 95.

² *Ludwig's Arbeiten*, 1873, p. 396.

³ *Pflüger's Archiv*, Vol. xxxvi. p. 252.

⁴ Tigerstedt und Santesson. Stockholm, 1886.

lymph formation in the light of the researches I have quoted, and come to the conclusion that transudation from the blood is brought about by an activity (in Folge einer activen Thätigkeit) of the cells of the capillaries. These authors further suggest that under many circumstances the flow of lymph is regulated by nervous influences and cite the experiments already made in Heidenhain's laboratory on this point. Thus Ostroumoff had shown that stimulation of the lingual nerve gives rise to a marked oedema on the side of the tongue of which the nerve is stimulated, and Rogowicz describes a somewhat similar effect on the lips on stimulation of the Ansa Vieussenii. Heidenhain in fact had ascribed the "pseudomotor" effect of stimulating the lingual nerve after dividing the hypoglossus to the increased flow of lymph that was produced at the same time into the tongue, and does not even regard the fact that the pseudomotor effect could be obtained after the death of the animal as militating against this explanation.

Unfortunately hardly any of these researches could be regarded as absolutely decisive and their interpretation would depend largely on personal predilection. Thus the flow of lymph on stimulation of the lingual nerve is associated with active hyperaemia of the tongue. Rogowicz obtained results on the leg which also were compatible with the filtration hypothesis. On the other hand the enormous variations observed in different experiments and by different experimenters lead Tigerstedt and Santesson to the opposite conclusion. All these experiments however were made on parts from which there is, under normal circumstances, no flow of lymph while the parts are at rest, and the facts that, to get any lymph at all for comparative measurement, we have to knead or passively move the limb, and that, in most experiments, curare has to be administered at intervals, introduce very considerable sources of error into the observations. Influenced by these considerations, Heidenhain some years later carried out a series of experiments on the lymph-flow from the thoracic duct¹. In these he investigated: first, the effect of changes in the blood-pressure and mechanical interference with the circulation on the lymph-flow; and secondly, the influence of the injection of various substances into the blood. In his latter part of the research, he confirms and amplifies the suggestion which was put forward in Rogowicz' paper, viz. that there exist substances which have a specific action in increasing the transudation from the blood-vessels, just as diuretics increase the

¹ *Pflüger's Archiv*, Vol. XLIX, p. 209.

secretion of urine by the kidney. To this class of bodies he has given the name of lymphagogues. From these results he comes to the conclusion that under normal circumstances filtration plays no part in the production of lymph.

With the questions of the mode of action of lymphagogues or of the effect of changes in the chemical composition of the blood on the flow of lymph we are not here concerned. In commencing the present research I had two objects in view; firstly, to investigate and if possible explain the remarkable results obtained by Heidenhain on the lymph-flow after obstruction of the aorta, vena cava, or portal vein; and secondly, in accordance with a suggestion contained in his paper, to seek once more for evidence of definite lymph-secretory nerves.

When the portal vein is ligatured, there is a large increase in the lymph-flow from the thoracic duct. The lymph at the same time becomes less concentrated and contains more and more red blood-corpuscles so long as the obstruction is continued. This increased flow Heidenhain looks upon as undoubtedly due to mechanical filtration. The capillary pressure is raised to a maximum, since there is a free access but no outlet for the blood. The resistance of the capillary walls no longer suffices to keep back even the red blood-corpuscles from passing through.

If on the other hand the aorta be obstructed above the diaphragm, the lymph-flow in Heidenhain's experiments underwent very little change in quantity (in one experiment being indeed slightly increased), although the arterial blood-pressure, as registered by a manometer in the femoral artery, had sunk almost to nothing. The lymph so produced contained less water and more proteids than normal lymph and he concluded that, since here the factor causing filtration, i.e. the blood-pressure, was absent, the lymph must have been formed by the capillary walls and that here we have to do with a process, not of filtration, but of secretion.

More paradoxical and difficult to explain is the effect produced by artificially obstructing the inferior vena cava just above the diaphragm. This measure caused a very large increase in the flow of lymph which was however more concentrated than normal lymph, thus differing from the ordinary lymph of venous obstruction. In this case there is an obstruction to the flow of blood from the veins, but the obstruction is not complete, while the arterial supply is largely diminished.

In one experiment of this description, after the obstruction, the lymph-flow from the thoracic duct rose from 3 cc. in 10 min. to 25 cc. in 10 min. At the same time, the percentage of solids in the lymph

rose from 4·8 before the obstruction to 6·6 after the obstruction. The coagulability of the lymph was at the same time affected, the lymph after the obstruction gradually losing more and more its coagulability. Coincident with this increase in the lymph-flow, we find a marked fall in the arterial pressure, from 125 to 37 mm. Hg. The experiment I have here quoted is a typical one and can be always repeated with success. The question now arises as to what is the source of this lymph. Does it come from the liver or from the intestines or other abdominal organs drained by the portal vein? The organs below the portal vein can be at once excluded. Heidenhain showed that obstruction of the vena cava, some distance below the entry of the hepatic veins, was absolutely without effect on the lymph-flow. On the other hand, he pointed out that if, directly after the death of the animal, the abdomen was opened and some coils of the intestine pressed with the hand, there was an enormous rush of lymph from the cannula in the thoracic duct. The liver on the contrary could be strongly pressed without squeezing a drop out of the cannula. He therefore concludes that the lymph obtained on obstruction of the inferior cava above the diaphragm has the same source as that produced by ligature of the portal vein and that it is derived from the intestines &c. which are drained by the portal vein.

What then is the reason of the difference in the composition of the lymph obtained under these two conditions? This was the question which I first sought to answer. Before however discussing this point, I will briefly describe the methods of experiment employed.

Method of Experiment.

My experiments were made solely on dogs (weighing from 6 kilos. upwards). These received, half an hour before the operation, an injection of 1 to 4 grains of morphia, and were anaesthetised during the experiment with A. C. E. mixture.

The thoracic duct was first prepared and a cannula similar to that recommended by Heidenhain was inserted into it. A cannula was then put into the central end of the left femoral artery, and connected with a Hürthle manometer. At intervals during the experiment a record was taken of the blood-pressure by this means. Then, if aorta or vena cava were to be obstructed, the right iliac artery or the right jugular vein were dissected out and ligatured. Samples of normal lymph were always collected for two or three intervals of 10 minutes before any experimental interference was begun. In cases where the splanchnics or spinal cord were to be cut or stimulated these were

dissected out from the back before putting the cannula into the thoracic duct. The methods used in these various operations were similar to those described in an earlier paper¹. In all cases the dogs had received no solid food for the 24 hours preceding the experiment.

The determinations of solids in lymph or blood were made in the usual way, by drying a weighed quantity (2 to 3 grams) of these fluids in a weighed porcelain crucible at 110° C. In determining the solids in lymph, this was always allowed to clot, and the solids estimated in the serum pressed out from the clot.

The effect on the lymph-flow of obstruction of the inferior vena cava above the diaphragm.

In my earlier experiments I found it easy to apparently confirm Heidenhain's observation as to the source of the lymph which flows from the thoracic duct and is obtained on obstruction of the inferior vena cava. In cases where the animal had died while the cava was still obstructed, on opening the abdomen a large flow of lymph from the thoracic duct was produced by squeezing two or three coils of intestine in the hand. Pressure on the liver on the other hand had no effect on the lymph-flow and one could at most squeeze out one or two drops of lymph in this way. The lymph therefore seemed to come from the same area as that which gives rise to the lymph obtained on obstruction of the portal vein, and the question which required investigation was the particular condition or conditions causing the difference in the composition of lymph in the two cases. If the abdomen be opened before obstructing the inferior vena cava, it will be seen that the obstruction of this vessel is followed, not by hyperaemia, but by a blanching of the intestines (Heidenhain). Since the obstruction to the flow of blood into the heart causes a great fall of arterial blood-pressure, this blanching may to some extent be caused by an active stimulation of the splanchnic nerves through the vasomotor centre, which is aroused to action by the low systemic pressure. I thought that possibly this excitation of the splanchnic nerves might not be entirely indifferent for the process of lymph secretion, and that indeed here the difference in the composition of the lymph might be caused by the activity of lymph-secretory nerves. I therefore planned two sets of experiments by which I hoped by artificial means to destroy the differences in the effects of obstructing the portal vein and inferior cava.

¹ "Observations on venous pressures and their relationship to capillary pressures." By W. M. Bayliss and E. H. Starling. *This Journal*, Vol. xvi. p. 159.

In the first set of experiments, both the splanchnics were divided from the back at the commencement of the experiment. Then after preparing the thoracic duct and femoral artery, the inferior cava was obstructed in two places by means of a double obturator. This was so arranged that the lower balloon would be just below and the upper balloon just above the opening of the hepatic veins. In this way, by making the obstruction more complete, and allowing a greater distension of the abdominal vessels, I thought the lymph so obtained might be ordinary venous obstruction lymph, i.e., more dilute than normal lymph. Such however was not the case. After division of both splanchnic nerves, the lymph obtained even on obstruction of the vena cava above and below the hepatic veins is more concentrated than the lymph obtained before obstruction. The sole difference in fact between this set of experiments and obstruction of the vein under normal circumstances is in the course of the arterial blood-pressure after the obstruction. In a normal dog the blood-pressure sinks, on obstruction of this vessel, to about one-third of its previous height, but remains fairly constant at this level for a considerable time. If however both splanchnics be divided, the blood-pressure sinks lower and lower during the whole time that the obstruction is continued, so that a dog dies sooner under these circumstances than when his splanchnics are intact. I give here protocols of two such experiments.

EXPERIMENT 1.

Division of splanchnics. Double obstruction of inferior cava.

April 27, 1893. Retriever about 20 kilos. Both splanchnics divided.

Time	Lymph	c.c. in 10 min.	Total Solids p.c.	Remarks
12.40'—50'	3.8 c.cm.	3.8	5.8	Lymph whitish. From 52'—55' double obturator introduced and both balloons distended.
55'—58'	10 c.cm.	33	6.6	
12.58'—1.8'.40"	62 c.cm.	58	7.7	Lymph transparent and almost colourless.
8'.40"—15'.40"	31.5 c.cm.	33		
15'.40"—19'	10 c.cm.	30	7.8	Lymph slightly reddish.
19'—23'.20"	10 c.cm.	23		More opaque.
23'.20"—28'.20"	8 c.cm.	16	7.77	At 1.25 B.P. almost nothing. Obstruction relieved at 1.28½.
29'—42'	10 c.cm.	7		Dog pulseless. Died at 1.40.

P.M. Found that upper balloon of obturator was just above hepatic veins and the lower just above renal veins. Rt. splanchnic only half cut through. Left great splanchnic divided. Small splanchnics on both sides intact. Clot in rt. heart.

All specimens of lymph clotted by 2 p.m.

EXPERIMENT 2.

Splanchnics divided. Obstruction of inf. vena cava.

May 1, 1893. Dog about 7 kilos. Splanchnics on both sides divided. Left fem. art. to H. manometer. Cannula in thoracic duct.

c.c. in 10 min.	Time	Lymph	Solids in lymph p.c.
1.3	12.0—12.15 = 2	c.cm. (with pressure on abdomen). Opalescent, yellowish	5.4
		At 12.23 obturator introduced and both balloons distended.	
6.5	20'—30' = 6.5	c.cm. Reddish towards end	6.6
		At 12.30 both balloons emptied, obturator left in place.	
9	30'—35' = 4.5	c.cm. (with slight pressure)	6.6
7	35'—40' = 3.5	c.cm. with slight pressure, rather bloody.	
		At 42' both balloons distended again.	
7.5	40'—50' = 7.5	c.cm.	6.6
		(Intestines very congested and venous.)	
11	50'—55' = 5.5	c.cm.	
		Water let out of both balloons at 55'.	
5.5	12.55—1.5 = 5.5	c.cm.	6.8
7	1.5—1.10 = 3.5	c.cm. (with pressure)	
		At 1.11 upper balloon distended. B. P. at once fell as low as before.	
7.5	1.12—1.22 = 7.5	c.cm. (Dog dying)	6.3
8	22'—32' = 8	c.cm. (Dog dead)	6.6

P.M. Found upper balloon on level with hepatic veins, occluding them completely. Lower balloon below renal veins. Intestines and stomach very congested. Both splanchnics completely divided. A little fluid in serous cavities. Retroperitoneal glands and ant. mediastinal glands swollen and oedematous.

All specimens of lymph clotted by end of experiment.

It will be seen that, in the first of these, the obstruction gave rise to an enormous flow of lymph, while the solids in the lymph rose from 5.8% to 7.8%. In Exp. 2, in which the division of the splanchnics was more complete, the lymph was increased only moderately by the

obstruction, but here again the solids rose from 5.4% to 6.8%. In repeating these experiments, one may, as I did at first, fall into error, either in consequence of the obturator being placed too low or of some injury to a large lymphatic trunk in dissecting out the splanchnic nerves. In two of my earlier experiments I injured a large lymphatic in dissecting out the left splanchnic nerve, or included it in the ligature and so obtained no increase of lymph on obstruction of the cava. I may mention too that section of the vagi was without influence on the effects of this obstruction, so that I concluded that a specific nerve-influence was not concerned in this increased production of lymph.

This conclusion was borne out by a second set of experiments in which I combined obstruction of the portal vein with stimulation of the splanchnic nerves, both with cord intact and cord divided. I need only quote one of these experiments.

EXPERIMENT 3.

Obstruction of portal vein. Stimulation of splanchnics.

May 5, 1893. Dog about 8 or 9 kilos. Cannula in thoracic duct. Both splanchnics on electrodes. Portal vein &c. (in transverse fissure) on "Ligaturstab."

c.c. in 10 min.	Time	Lymph	Solids in lymph p.c.
1.8	11.55—12.10 = 2.8 c.cm.	(with pressure) very bloody	6.4
2.7	12.10—25' = 4 c.cm.	(not quite so bloody)	6.2
	(From 12.12—25' splanchnics excited. R. A. 10, 9, 8.)		
	Both vagi cut at 12.20.		
3	25'—30' = 1.5 c.cm.		
7	30'—40' = 7 c.cm.		5.3
	(From 12.31—45' splanchnics excited. R. A. ¹ 7, and portal ligature pulled tight at 12.31. Two intermissions of 45" in the excitation during this 10 mins.)		
6.5	40'—50' = 6.5 c.cm.		5.3
	(At 42' portal vein released.)		
	At 45' excitation of splanchnics stopped.		
5	50'—60' = 5 c.cm.		
5.3	1.0—1.15 = 8 c.cm.		5.8
	From 1.0—1.5, portal vein obstructed.		
	From 1.0—1.15 splanchnics stimulated (R. A. 1) with 6 intermissions of half-a-minute.		

P.M. Intestines very congested.

¹ Here, and in other experiments, R. A. stands for distance of secondary from primary coil.

It will be seen that obstruction of the portal vein had its usual effect, i.e. an increased flow of lymph containing a smaller proportion of solids than the normal; the solids in this experiment fell from 6·4% to 5·3%, and stimulation of the splanchnics seemed to have no effect on the appearance or composition of the lymph.

As I had already learnt that tissue-fibrinogens might act as lymphagogues, it seemed possible that perhaps obscure changes in the fibrinogens of the blood which was dammed up in the liver and intestines, might be responsible for the increased flow of concentrated lymph. This idea however had to be discarded when it was found that total defibrination of the blood did not disturb in the slightest degree the results of the obstruction of the inferior cava. A dog was bled until no more blood could be obtained and the blood defibrinated and reinjected slowly into the jugular vein. This procedure was repeated 5 or 6 times. After the 5th time, the blood was absolutely uncoagulable¹; care must be taken in this experiment to keep the blood warm during defibrination, in order not to chill the animal on reinjecting it. In a dog whose blood has thus been defibrinated, obstruction of the cava above the diaphragm gives rise to increase in the lymph-flow, and the lymph thus obtained is more concentrated than before the obstruction.

Several other hypotheses proved equally futile when put to the test of experiment. Almost in despair I thought of applying a further test to Heidenhain's view as to the source of the lymph obtained under these circumstances. I had noticed that, after death from obstruction of the inferior vena cava, the lymphatics in the hilus of the liver were very distended, and it seemed possible that perhaps after all the liver was responsible for the increased flow of concentrated lymph, and that I had during these months been struggling with a chimera.

The researches of v. Fleischl, Asp and Budge have shown that

¹ This procedure has practically no effect on the lymph-flow, the amount of lymph obtained in 10 minutes after the blood has been defibrinated being the same as at the commencement of the experiment. Thus in one experiment the amounts were

Before defibrination 1·5 c.c. in 10 mins.

After defibrination 2 e.c. in 10 mins.

In another experiment they were

Before defibrination 7 e.c. in 10 mins.

After defibrination 9 e.c. in 10 mins.

I have purposely chosen two dogs in which the normal flow was minimal and maximal. The only effect of the defibrination is that the gradual diminution of the lymph-flow, which ordinarily takes place in the course of an experiment, seems to be checked.

the lymphatics of the liver take various courses, some accompanying the hepatic vein and others joining the subperitoneal and diaphragmatic plexuses. The largest of them however leave the liver at the portal fissure, and I thought that by ligature of these one might reduce the effects of obstruction of the cava to a minimum, supposing that the liver was really the source of the lymph. On trying the experiment I found to my surprise that obstruction of the inferior cava was absolutely without effect on the lymph-flow, if one had previously ligatured the portal lymphatics. I repeated this experiment many times but always with the same results, and was finally persuaded that the whole increase of lymph obtained on obstruction of the inferior cava above the diaphragm is derived from the liver.

Since this point is extremely important, I give protocols of four experiments in which the portal lymphatics were ligatured. In the first experiment a ligature was put *loosely* round all the structures in the portal fissure (lymphatics, hepatic artery and biliary duct) with the exception of the portal vein. Then after a cannula had been placed in the thoracic duct, the inferior cava was obstructed above the liver in the usual way. There was at once an increase in the amount of lymph from 2 c.cm. to 10 c.cm. in the 10 minutes, and the solids at the same time rose from 6.46% to 7.102%. The ligature in the portal fissure was now pulled tight, and at once the lymph-flow fell to 4 c.cm. and then to 3 c.cm. in the 10 minutes, the proportion of solids falling at the same time to 6.81%. The obturator was then withdrawn. A second obstruction some time later was without effect on the lymph-flow.

EXPERIMENT 4.

Obstruction of inferior cava. Ligature of liver lymphatics.

May 8, 1893. Dog about 10 kilos. Ligature loosely round structures in portal fissure, excluding portal vein.

c.c. in 10 min.	Time	Lymph	Solids p.c.
2.7	11.45—12.0 = 4 c.cm.	opalescent, colourless. Clots directly	6.46
		Blood sample (1) at 11.50. The serum contains	7.33
4	12.0—12.5 = 2 c.cm.		
		At 12.6 obturator introduced and distended in I. V. C.	
4	12.5—15' = 4 c.cm.		
		At 12.12 obturator released, and moved one inch higher and redistended.	
		Blood pressure sank immediately.	

8	12.15—25' = 8 c.cm.	6·96
10	25'—35' = 10 c.cm.	7·102
	Blood sample (2) taken at 12.34. Serum contains	7·02
	At 12.36 ligature in portal fissure tied. (Liver lymphatics thus obstructed.)	
4	12.35—50' = 6 c.cm. Clearer	6·96
3	50'—1.0 = 3 c.cm.	6·81
	At 1.1, water let out of obturator.	
	Blood sample (3) at 1.8. The serum contains	7·15
	Blood sample (4) at 1.14. The serum contains	7·12
2	1.0—1.15 = 3·5 c.cm.	6·59
	At 1.16, obturator introduced again and distended.	
1·7	1.15—30' = 2·5 c.cm.	
2	30'—40' = 2 c.cm., slightly reddened	6·40

Dog then killed. P.M. Obturator found just above liver, and occluding hepatic veins. Lymphatics in portal fissure enormously distended, and some extravasation of lymph. Lymphatics of intestine not distended, and no lymph obtained on squeezing them.

Blood samples (1) and (2) clotted soon: (3) and (4) however clotted slowly and were only imperfectly clotted 2 hours later, when they were centrifuged and the serum obtained for estimating solids.

EXPERIMENT 5.

Obstruction of inferior cava. Ligature of liver lymphatics.

May 10, 1893. Dog about 10 kilos. Cannula in thoracic duct at 11 a.m. Duct very small. No flow of lymph (even on pressure) between 11 and 12. Ligature loosely round structures in portal fissure, excluding portal vein. At 11.55, inferior vena cava obstructed above diaphragm.

c.c. in 10 min.	Time	Lymph
9	12.0—12.10 = 9 c.cm.	(a little reddish towards end).
	At 12.6 water let out of obturator.	
4·6	12.10—20' = 4·6 c.cm.	
	At 12.20 obturator blown up again.	
6	20'—25' = 3 c.cm.	
	At 12.25 ligature in portal fissure pulled tight.	
5	25'—30' = 1 c.cm.	
2	30'—40' = 2 c.cm.	
	Water let out of obturator at 40'.	
2	40'—50' = 2 c.cm.	
	Dog killed.	

P.M. Lymphatics of liver very distended. The ligature in the portal fissure was then loosened, and afterwards first the intestines and then the liver were squeezed.

6 c.cm. of lymph obtained on squeezing intestines contained 4.5 per cent. solids.

6 c.cm. of lymph obtained on squeezing liver contained 6.0 per cent. solids.

The latter was more transparent than the lymph obtained from the duct by squeezing intestines.

This experiment is essentially similar to experiment 4. At the end of the experiment however I thought of testing the relative compositions of liver and intestinal lymph, and found, as is shown above, that the liver lymph was much richer in solids than the intestinal lymph.

EXPERIMENT 6.

Obstruction of inferior cava, and liver lymphatics.

May 12, 1893. Dog about 8 kilos. Structures in portal fissure (excluding portal vein) ligatured with slip-knot at 11.5.

c.c. in 10 min.	Time	Lymph
1.3	10.55—11.10 =	2 e.cm.
1.2	11.10—25' =	1.8 c.cm.
	Between 25' and 30', introduced obturator and distended it above diaphragm.	
2	11.30—40' =	2 e.cm.
1.2	40'—50' =	1.2 e.cm.
	At 11.50 ligature in portal fissure released.	
1.5	11.50—12.0 =	1.5 e.cm.
	Dog killed.	

At P.M. some bloody fluid in peritoneal cavity.

Lymphatics of intestine not distended.

Some of the liver lymphatics distended. Others were ruptured.

In this experiment the ligature round the portal lymphatics was tightened before the vein was obstructed, and we find that in this case the obstruction was absolutely without effect. I had hoped to be able to ligature and release the lymphatics at will. This however proved impossible. The delicate lymphatics were too torn and crushed by the ligature to allow of a restoration of their perviousness. Cp. Exp. 10.

EXPERIMENT 7.

Obstruction of inferior cava and liver lymphatics.

May 22, 1893. Young dog about 10 or 12 kilos. Cannula in thoracic duct. Left femoral art. to Hürthle manometer. Rt. jugular vein prepared for obturator.

c.c. in 10 min.	Time	Lymph	Solids p.c. in lymph serum
2.5	11.10—11.30	= 5 c.cm. Colourless, opalescent.	
3	30'—45'	= 4.5 c.cm.	4.30 (colourless)
From 35' to 45' portal vein dissected out, and the other structures in the transverse fissure ligatured. Abdomen then closed.			
2.2	11.50—60'	= 2.2 c.cm., whitish	4.95 (serum colourless)
At 12.5 obturator introduced into vein, and distended at 12.7.			
2	12.5—15'	= 2 c.cm., slightly bloody	} rather clearer 5.03 (serum light yellow)
2	15'—30'	= 3 c.cm., ,, ,,	
At 12.30, water let out of obturator.			
4.8	30'—40'	= 4.8 c.cm., more bloody	5.39 (reddish yellow)
4.2	40'—50'	= 4.2 c.cm., not so bloody	5.38 (yellow)
At 12.50 obturator reintroduced and distended at 12.53.			
4	12.50—1.0	= 4 c.cm.	5.09 (serum yellow)
4.5	1.0—1.10	= 4.5 c.cm.	(all lymph sera quite clear)

Dog killed by bleeding from femoral. Lymphatics of liver very distended. Obturator just above liver. Intestines anaemic. All specimens of lymph clotted normally.

This experiment is quoted to show that the operation of dissecting out the portal vein and ligaturing the structures in the portal fissure (including lymphatics) has very little effect on the normal flow of lymph. Its effect is only noticed when the inferior cava is obstructed.

It has been raised as a possible objection to the above results, that, in ligaturing or dissecting out the portal lymphatics, I may have obstructed or torn some large lymphatic from the intestines, and thus got no effect from obstruction of the inferior cava. I think however the details of the experiments given above would sufficiently dispose of this

objection. Moreover in some cases I have inadvertently occluded or partially occluded the portal vein in tightening the ligature round the lymphatics, and have then invariably got an increased flow of bloody lymph with lessened percentage of solids, showing that the way from the intestinal lymphatics was still patent after ligature of the portal lymphatics.

The converse experiment, namely the occlusion of the lymphatics from the intestines &c., I could not carry out. A total extirpation of the organs drained by the portal vein was also impossible, since one would in this way cut off the chief blood-supply from the liver, and also divide the lymphatics running from the liver. I thought however my conclusion would be strengthened if it was found that extirpation of the greater part of the intestine had no influence on the effects of obstructing the inferior cava. In the following experiment it will be seen that extirpation of $6\frac{1}{2}$ feet of small intestine had in fact no effect in diminishing the lymph-flow obtained under these circumstances. It will be observed too that by pressure on the liver at the end of the experiment it was not possible to drive out any lymph by the thoracic duct.

EXPERIMENT 8.

Extirpation of Intestine. Obstruction of inferior vena cava.

May 29, 1893. Dog about 12 kilos. Cannula in thoracic duct. Left femoral art. to H. manometer.

c.c. in 10 min.	Time	Lymph	Solids p.c. in lymph serum
5	2.35—50' = 7.5 c.cm.,	reddish yellow	6.06
	Between 2.50 and 3.5 whole of small intestine (except duodenum) excised. The excised piece was $6\frac{1}{2}$ feet long.		
4.7	2.50—3.5 = 7 c.cm.		
4.2	3.5—3.12 = 3 c.cm. (with pressure)		6.52
4.1	12'—18' = 2.5 c.cm.		
	Between 12' and 18' obturator introduced into inferior cava and distended.		
5	18'—25' = 3.5 c.cm. (Obturator too low. No effect on B. P.)		
	At 3.22 both vagi divided.		
	At 3.25 obturator moved 1 inch higher and redistended.		
22	25'—30' = 11 c.cm. (B. P. very low)		6.93
20	30'—35' = 10 c.cm.		
12.8	35'—40' = 6.4 c.cm.		7.35
	At 3.40 water let out of balloon.		

6	40'—50' = 6 c.cm.	
4	50'—60' = 4 c.cm.	6.48
	At 4 p.m. obturator introduced again and distended.	
14	4.0—4.7 = 10 c.cm., more bloody	7.03
12.7	4.7—4.15 = 10.2 c.cm.	
10	15'—25' = 10 c.cm.	

P.M. Found I had left in abdomen the stomach and one foot of duodenum and one foot of large intestine. Liver extremely congested. On squeezing hardly a drop of lymph came out of the cannula.

All specimens of lymph serum quite clear and light yellow.

It might be thought that the effect of ligaturing the structures in the portal fissure might be really due to ligature not of the lymphatics but of the hepatic artery. That this objection is groundless, is shown by the following experiment, in which the hepatic artery was ligatured by itself but without any effect on the lymph-flow under any circumstances.

EXPERIMENT 9.

Ligature of hepatic artery. Subsequent obstruction of inferior cava.

June 16, 1893. Dog about 9 kilos. Cannula in thoracic duct. Left fem. artery to H. manometer.

c.c. in 10 min.	Time	Lymph	Solids in lymph p.e.
7	2.50—3.0 = 7 c.cm.,	reddish yellow, cloudy	
4.4	3.0—3.15 = 6.6 c.cm.,	reddish	6.93
	Between 3.0 and 3.10 abdomen opened and hepatic artery ligatured.		
2.6	3.15—30' = 4 c.cm.,	less bloody towards end.	
3.4	30'—40' = 3.4 c.cm.	No blood. Yellowish. Almost clear	7.10
	At 3.55 obstructed vena cava above liver.		
14	3.55—4.2 = 10 c.cm.,	clear, slightly reddish	7.00
16	4.2—4.8 = 10 c.cm.,	yellowish, clear	7.14
	At 4.8 water let out and obturator withdrawn.		
14	4.8—4.15 = 10 c.cm.,	slightly more cloudy	
6	15'—25' = 6 c.cm.,	reddish	6.61
6	25'—40' = 9 c.cm.,	bloody.	6.61

Dog then killed by bleeding. Blood clotted normally.

At P.M. found hepatic artery ligatured. Everything else normal. All lymphis clotted.

How then is it that although the whole increase of lymph-flow produced by obstruction of the inferior cava above the liver, comes from the liver, yet pressure on this organ fails to drive a drop of lymph out of the cannula in the thoracic duct, whereas a mighty flow is produced by squeezing some coils of intestine?

To throw light on this point I performed the following experiment. It is well known that a solution of indigo-carmin injected under pressure into the biliary ducts, quickly enters the lymphatics of the liver. I therefore put a cannula in the thoracic duct of a dog, and then killed him by bleeding. Some minutes later, the abdomen was opened and a cannula tied into the bile duct. This cannula was connected with a burette containing a half per cent. solution of indigo-carmin in normal saline solution. On connecting the top of the cannula with a syringe the fluid could be made to flow slowly into the bile duct. After a short time blue lymph began to drop from the cannula in the thoracic duct.

The injection was then stopped, and it was found that a large flow of blue lymph could be caused by squeezing the intestines, whereas pressure on the liver was practically without effect.

On examining the abdominal organs it was found that the portal lymphatics were distended with blue lymph, which also filled large lymphatic trunks in the mesentery of the duodenum. The small intestines themselves were not stained. On repeating the experiment again it was discovered that *careful* squeezing of a single coil of intestine had no effect on the lymph-flow. Before, in squeezing several coils, I had dragged or pressed on the lymphatics in the upper part of the mesentery and probably also in the cisterna and had so caused the rapid flow of lymph.

And exactly the same thing holds good for the lymph produced by obstruction of the inferior cava. If care be taken to limit the pressure to a single soil of intestine, so as not to drag or press on the large lymphatics which are in direct connection with the portal lymphatics, we obtain no increased flow of lymph from the thoracic duct.

The lymphatics in the liver seem to be protected by their solid framework from the effects of any pressure that may be applied to the liver, and hence has arisen the fallacy of ascribing the lymph produced by obstruction of the inferior cava to the intestines instead of to the liver.

If further proof were needed it is afforded by the following experiment, in which, during obstruction of the cava, the portal vein and

lymphatics were alternately compressed and released. It will be seen that with portal vein and lymphatics open the lymph is increased and more concentrated, with these vessels closed it at once becomes *diminished* and more dilute, although in the latter case the venous congestion in the intestinal area is much greater than in the former case. The lymphatics in this case were not dissected free from the portal vein, and hence are not destroyed or injured by the direct pressure or contact of the ligature.

EXPERIMENT 10.

Obstruction of portal vein and inferior cava.

June 2, 1893. Dog about 10 kilos. Ligature on "Ligaturstab" loosely round structures in small omentum (portal vein &c.).

c.c. in 10 min.	Time	Lymph	Solids in lymph serum p.c.
2	12.15—25' = 2 c.cm.,	clear, almost colourless	5.61
		Between 25' and 28' obturator introduced into inferior cava and blown up. At 30', portal ligature pulled tight.	
3	12.30—40' = 3 c.cm.,	slightly red towards end	5.82
		At 40' portal ligature released and water let out of obturator.	
9	40'—50' = 9 c.cm.,	reddish	6.15
5.2	50'—60' = 5.2 c.cm.,	less red.	
4	1.0—1.5 = 2 c.cm.,	not red	6.09
		At 1.5 vena cava and portal vein &c. again obstructed.	
3.2	1.5—15' = 3.2 c.cm.,	slightly red towards end	5.71
5	15'—25' = 5 c.cm.,	very bloody	5.35
		At 25' portal ligature released.	
20	25'—30' = 10 c.cm.,	very red.	
22	30'—35' = 12 c.cm.	"	
20	35'—40' = 10 c.cm.	"	
17	40'—45' = 8.5 c.cm.		6.74
		At 45' portal ligature pulled tight.	
4.2	45'—52' = 3 c.cm.,	very bloody.	
		At 52' portal ligature released.	
13.6	52'—59' = 9.5 c.cm.		

I have proved that the increase of the lymph observed after obstruction of the vena cava above the diaphragm is entirely derived from the liver. We have now to enquire, why is the lymph produced in the liver increased under these circumstances, and why is it more concentrated than ordinary lymph?

In the first place there is no doubt that extreme venous congestion of the liver is produced by obstruction of the inferior cava above the diaphragm. If the dog be allowed to die while the cava is still obstructed, the liver will be found to be swollen, hard and hyperaemic. And if the pressures in the portal vein and inferior cava be measured it will be found that the obstruction causes a large rise of pressure in both vessels. There is therefore, as has been already shown, a large rise of intracapillary pressure in the liver (cp. Exp. 2*)¹. In Exp. 2* the pressure in the portal vein rose from 90 to 240 mm. MgSO₄ solution and that in the iliac vein from 51 to 240, on obstruction of the inferior cava. At the same time the equalisation of the pressures in the portal vein and cava shews that the velocity of blood through the liver is largely diminished. We can therefore ascribe the increased flow of lymph from the liver only to the rise of pressure in the capillaries of this organ.

This conclusion is confirmed by the fact that the amount of lymph produced is proportional to the intracapillary pressure. If, while the vena cava is obstructed, the aorta be also obstructed, there is at once a diminution of the lymph-flow. This is shown in the following experiment.

EXPERIMENT 11.

Obstruction of inferior vena cava and thoracic aorta.

June 7, 1893. Dog about 10 kilos. Cannula in thoracic duct. Left fem. art. to H. manometer. Rt. iliac artery and extl. jugular vein prepared for obturators.

e.c. in 10 min.	Time	Lymph	Solids in lymph p.e.
2.4	2.55—3.20 =	6 c.cm., whitish.	
2.25	3.20—30' =	2.25 c.cm.	5.30
	Between 30' and 40', both obturators introduced.		
	At 40' obturator in vena cava distended above diaphragm.		
12	40'—50' =	6 c.cm. (i.e. 12 in 10 mins.)	6.00
	At 45' aorta obstructed.		
8.2	45'—55' =	8.2 c.cm. (in 10 mins.)	6.85
	At 55' aorta released.		
16	55'—60' =	8 c.cm. (= 16 in 10 mins.)	6.87
	At 60' water let out of vein obturator.		
6	4.0—4.10 =	6 c.cm.	
	Dog died about 4.6.		

¹ Experiments distinguished by an asterisk (2*) allude to those given in the preceding paper. "Observations on Venous Pressures, &c." By W. M. Bayliss and E. H. Starling.

It will be seen that during the first 5 minutes after obstruction of the inferior cava 6 c.cm. of lymph are obtained, i.e. at the rate of 12 c.cm. in 10 mins. Under ordinary circumstances we should expect to obtain more lymph in the second 5 mins. than in the first 5 mins. after obstruction of the cava. In this experiment however the aorta was obstructed, and the lymph fell instead of rising, so that only 8.2 c.cm. were obtained in 10 mins. The aortic obstruction was then removed and at once the lymph-flow was increased so that 8 c.cm. were obtained in the next 5 minutes (at the rate of 16 c.cm. in 10 minutes). During the obstruction of the aorta, the engorged veins have an opportunity to empty themselves of their contained blood, the pressure in the liver capillaries falls, and with it falls also the amount of lymph produced.

There is thus, in the liver at any rate, a direct proportionality between the intracapillary pressure and the formation of lymph. We have now to enquire how far this proportionality between blood-pressure and lymph-production is borne out by other experimental modifications of the circulation in the abdominal organs.

Obstruction of the Thoracic Aorta.

Heidenhain showed that, after obstruction of the thoracic aorta, the lymph-flow from the thoracic duct was generally diminished to some extent, but the diminution was in no way proportional to the reduction of arterial blood-pressure produced by the obstruction. The lymph-flow might continue from one to two hours after the aorta had been obstructed. In two experiments indeed he obtained a transitory increase in the amount of lymph after obstruction of the aorta. This absence of proportionality between the arterial pressure and the amount of lymph obtained leads Heidenhain to the conclusion that the lymph-production is not a function of the intracapillary pressure, but involves a secretory activity of the endothelial cells. He is further strengthened in this conclusion by the fact that, under these circumstances, the lymph changes in quality, presenting a whitish appearance and containing a larger percentage of solids.

In the preceding paper we have shown that we are not warranted in assuming that the pressure in the capillaries of the abdominal organs is necessarily proportional to, or is even altered in the same direction as, the arterial blood-pressure. Before coming to any conclusion as to the interpretation of the results produced on the lymph by obstruc-

tion of the aorta, we must first investigate more nearly the condition of the circulation in the abdominal organs.

In my experiments I have found that obstruction of the thoracic aorta produces a diminution in the amount of lymph, the amount obtained after the obstruction varying from one-third to two-thirds of the normal quantity. I have not yet met with a case in which obstruction of the aorta produced even a temporary increase in the lymph-flow. On the other hand, the amount of solids in the lymph has been always increased. The question now arises: What organs form the source of the lymph so obtained and how is the intracapillary pressure in these organs affected by the obstruction of the aorta? On investigating the latter point, it is found that obstruction of the aorta causes a large fall of pressure in the arteries below the point of obstruction, a moderate fall in the portal vein and no fall at all or a slight rise in the vena cava (cp. Exp. 7*). There is therefore a large fall of pressure in the capillaries of the area which is drained by the portal vein, whereas in the liver the pressure may be unaltered or even slightly raised. If then lymph-production is determined by intracapillary pressure, the lymph obtained after obstruction of the aorta must arise entirely or nearly entirely in the liver. In the following experiment, I therefore, after obstructing the thoracic aorta, ligatured the lymphatics in the portal fissure. It will be seen that, by this means, the flow of lymph from the thoracic duct was abolished, showing that no lymph was being produced in the intestines. That the intestinal lymphatics were still patent is shown by the fact that, on relieving the obstruction of the aorta, an increased flow of lymph was at once obtained.

EXPERIMENT 12.

Obstruction of thoracic aorta before and after ligature of liver lymphatics.
June 27, 1893. Dog about 10 kilos. Cannula in thoracic duct.

c.c. in 10 min.	Time	Lymph	Solids p.c.
2	12.0—12.10 =	3 c.cm., transparent	6.18
3.6	10'—40' =	11 c.cm. (some lost), yellow.	
	(Between 12.10 and 40' a ligature put loosely round liver lymphatics in portal fissure, and aortic obturator introduced through rt. iliac artery. Fem. art. connected with H. manometer.		
2.6	12.40—50' =	2.6 c.cm., transparent, yellow	6.74
	At 51' aortic obturator distended.		

1.4	50'—60' = 1.4 c.cm.	
1.8	1.0—1.25 = 4.6 c.cm.	6.98
At 1.26 a little more fluid injected into obturator.		
2	25'—35' = about 2 c.cm. (some spilt)	
Aortic balloon burst at 1.35. Taken out.		
3.8	35'—45' = 3.8 c.cm., rather bloody	6.52
4.4	45'—50' = 2.2 c.cm., „ „	
Between 45' and 50' obturator introduced, and distended at 50'.		
3	1.50—2.0 = 3 c.cm., slightly reddish.	
2.4	{ 2.0—10' = 1 c.cm., almost colourless.	6.43
	{ 10'—20' = 3.8 c.cm. (a small clot removed from cannula)	
At 2.20 portal lymphatics ligatured.		
1.8	2.20—30' = 1.8 c.cm. (with strong pressure on abdomen ; without pressure no lymph-flow at all	6.29
0.3	30'—60' = 1 c.cm. (with strong pressure)	6.27
At 3.0 water let out and aortic obturator removed.		
2	3.0—3.10 = 2 c.cm.	
2.8	10'—45' = 10 c.cm., very bloody	6.54
Dog killed.		

So, after obstruction of the aorta, as after obstruction of the inferior cava, the chief lymph-flow is derived from the liver, or the lymph so obtained is more concentrated than the normal mixed lymph obtained before the obstruction.

The influence of the pressure in the abdominal capillaries on the flow of lymph is further illustrated by the following experiment, in which the thoracic aorta was first obstructed and 30 mins. later the inferior vena cava was obstructed above the diaphragm. The lymph, which was much diminished in consequence of the aortic obstruction, rose again gradually after the obstruction of the cava, as the vessels became gradually fuller.

EXPERIMENT 13.

Obstruction of aorta and, later on, of vena cava.
July 31, 1893. Dog about 10 kilos. (Rather cold.)

c.c. in 10 min.	Time	Lymph
1	2.55—3.5	= 1 c.cm., clear, colourless.
1.2	3.5—15'	= 1.2 c.cm.
At 3.16 aorta obstructed above diaphragm.		
0.6	3.15—25'	= 0.6 c.cm.

2 drops	25'—40' = 3 drops.
	From 40' to 45' introduced obturator into inf. vena cava, and distended it above diaphragm.
0·26	45'—60' = 0·4 c.cm.
1·1	4.0—4.20 = 2·2 c.cm.
	At 4.20 aorta released.
7	4.20—30' = 7 c.cm., bloody at first, whitish towards end.
9	30'—40' = 9 c.cm., clear, red.
	At 4.40 water let out of vein obturator.
8·1	40'—45' = 4 c.cm., less red.
4·5	45'—55' = 4·5 c.cm., almost colourless.
3·4	4.55—5.5 = 3·4 c.cm., colourless, transparent.

The course of the pressure-curves in the vessels of the abdominal organs is given in Exp. 7*, where it will be seen that the pressures in the portal vein and vena cava rise steadily for some time after the obstruction of the cava. Now in this experiment, the only thing which can account for the increased lymph-flow is the rise of intracapillary pressure in the liver and perhaps, to a slight extent, in the intestines. The circulation is practically at a standstill, and the velocity of the flow of blood through the abdominal organs is nothing at all, as shown by the fact that the pressures in the splenic and iliac veins are the same.

Obstruction of portal vein.

When the portal vein is ligatured (and in this case it is immaterial whether it be ligatured alone or together with all the other structures in the portal fissure), the lymph-flow from the thoracic duct is increased and the lymph at the same time becomes more watery. As we have already pointed out, this obstruction causes an enormous rise of pressure in the portal vein and in the capillaries of the intestines, &c., so that haemorrhage per diapedesim takes place and the lymph contains a number of red blood-corpuscles¹.

Obstruction of the renal veins.

Ligature of both renal veins, or obstruction of the inferior vena cava just above the renal veins, gives rise, under normal circumstances, to a moderate increase in the lymph-flow from the thoracic duct. The

¹ If the obstruction be only partial, an increased flow of lymph is obtained, which may be perfectly colourless and free from red corpuscles. Venous congestion does not necessarily give rise to diapedesis of red corpuscles, unless the rise of pressure so induced is very great.

lymph may, at the same time, become bloody, in consequence of the hæmorrhages in the substance of the kidney which are thus produced. The following experiment shows the effect on the lymph-flow and composition of obstructing first the renal veins and later on the portal vein.

EXPERIMENT 14.

Ligature of renal veins, and then of portal vein.

Oct. 17, 1892. Dog about 8 kilos. Ligatures loosely round both renal veins. Cannula in thoracic duct.

c.c. in 10 min.	Time	Lymph	Solids p.c.
6	1.0—1.10 =	6 c.cm., opalescent, yellowish.	
3.2	10'—30' =	6.5 c.cm.	5.2
2.5	30'—40' =	2.5 c.cm.	
2.5	40'—50' =	2.5 c.cm.	
At 1.52 both renal veins tied.			
4	1.55—2.5 =	4 c.cm., redder.	
4	2.5—15' =	4 c.cm.	
4.5	15'—25' =	4.5 c.cm.	4.9
At 2.25 portal vein, hepatic art. etc. ligatured in portal fissure.			
12	2.30—40' =	12 c.cm.	
12	40'—55' =	18 c.cm.	4.7
8	55'—3.5 =	8 c.cm.	

The effects of the obstruction of the cava above the renal veins are much intensified if both splanchnic nerves be previously divided. Thus in one experiment, after both splanchnics had been divided, 2.2 e.cm. of lymph were obtained in 10 mins. from the thoracic duct. The serum of this contained 5.86% of solids. The vena cava was then obstructed just below the hepatic veins. In the next 10 mins. the amount of lymph rose to 11 e.cm. It was bloody and the serum only contained 5.34% solids. This effect of section of the vasomotors is similar to that obtained by Emminghaus and by Cohnheim on the hind limb of the dog.

We thus see that in all these mechanical interferences with the circulation an increased flow of lymph is conditioned simply and solely by increased capillary pressure. There is one question however, that I have not yet touched upon, and which is of considerable importance. I mean the varying composition of the lymph obtained under these different conditions and especially the fact that, from the liver, we

obtained on venous or aortic obstruction, a lymph more concentrated than the lymph normally obtained from the thoracic duct.

Under all the conditions in which we can obtain a liver-lymph free from intestinal lymph, we find that the former is more concentrated than normal mixed lymph. This is well illustrated by Exp. 5, in which the liver-lymph contained 6% of solids and the intestinal lymph only 4.5% solids. The simplest way of explaining these differences is to look upon them as due to differences in the permeability of the filtering medium. The more permeable the medium the greater is the effect of changes in the pressure of the filtering fluid and the greater is the ease with which dissolved proteids pass through it. Thus the capillaries of the limbs have only a small permeability. The amount of transudation through them is but little affected by fairly large changes in the pressure of the blood within them, although, as Rogowicz has shown, they are so affected. At the same time they allow but a small proportion of proteids to pass through, the lymph only containing from 2% to 4% total solids. The intestinal capillaries are more permeable, so that the normal blood-pressure in them suffices to cause a transudation which is more than enough to fill the lymph-spaces of the tissues, and the excess of lymph passes off and gives rise to a constant flow through the thoracic duct. The lymph-flow from them is very appreciably affected by changes in the pressure of the blood within them. They are more permeable for proteids than the limb capillaries, so that the lymph from them contains from 4.5% to 6% proteids.

Highest in the scale of permeability come the liver capillaries. From these, there is under normal circumstances probably a flow of lymph, although the blood-pressure in them is very little above zero. The lymph which is obtained from them contains from 6 to 8% proteids and is in fact almost as concentrated as the plasma within the vessels. They are extremely sensitive to changes in pressure. A rise of pressure to 200 mm. water, which is probably less than the normal pressure in the intestinal capillaries, suffices to produce a colossal transudation, giving rise to the great increase of lymph-flow from the thoracic duct, which we have studied above.

It is probably to changes in the permeability of the vessel-wall, as Colnheim has suggested, that are due many of the important features of inflammation. Keep a dog's foot in water at 60° C. for five min. and the vessels undergo an alteration; their permeability is increased; we have in fact reduced the limb-capillaries to the condition of the

hepatic capillaries. The normal pressure to which they are subjected suffices now to cause a transudation which is too great to be carried off by the lymphatics and therefore accumulates in the interstices of the tissue, giving rise to oedema. The greater permeability is evidenced moreover by the greater concentration of the lymph so produced, due to the larger amount of proteids it contains. Now too the limb-capillaries react in a marked manner to changes in the pressure of the blood they contain. Cohnheim and Jankowsky have shown that the lymph flowing from an inflamed limb is markedly affected by influences (such as section of vaso-motor nerves or obstruction of the veins of the limb) which, applied to the sound limb, would only cause slight and doubtful changes in the amount of lymph to be obtained.

There is one other factor however, which may be of importance in determining the concentration of the lymph obtained from different parts. I refer to the varying concentration of the blood-plasma in different parts of the circulation. Hamburger has shown that every chemical change in the plasma occasions an interchange of material between plasma and corpuscles. Thus addition of acids to blood causes the amount of proteids in the plasma or serum to be increased at the expense of the red blood-corpuscles. Addition of alkalies has the reverse effect. In this respect, carbon dioxide acts like an acid, so that the plasma of venous blood contains more proteids than would the plasma of the same blood arterialised. Now the chief blood-supply of the liver is venous, and the plasma of the blood circulating in the hepatic capillaries would therefore be more concentrated than the plasma in any other capillaries of the body. This factor at any rate probably accounts for the increased concentration of the lymph obtained by Heidenhain when aorta and portal vein were obstructed at the same time. In this case there is a small flow of blood into the intestinal capillaries, but the outflow is almost entirely blocked, so that the blood in the intestinal capillaries must become extremely venous. In the following experiment the thoracic aorta and portal vein were occluded simultaneously, and it will be noticed that the three first portions of lymph obtained after the obstruction were milk-white and contained a larger percentage of solids than the lymph before the obstruction. In this experiment, the flow of lymph from the liver was cut off, if one may regard ligature of the portal lymphatics as equivalent to a complete shutting off of the liver-lymph, so that the concentrated lymph obtained must have come from the intestines and other organs drained by the portal vein.

EXPERIMENT 15.

Obstruction of portal vein and thoracic aorta.

May 26, 1893. Young dog about 10 kilos.

c.c. in 10 min.	Time	Lymph	Solids p.c.
3	11.50—12.0 = 3 c.cm.,	clear, opalescent	5.69
		Between 12.0 and 12.7 ligature (on ligature rod) put loosely round everything in portal fissure (portal vein, lymphatics &c.).	
3	12.0—12.10 = 3 c.cm.		
		At 12.28½ aorta occluded and portal ligature pulled tight.	
1	12.30—40' = 1 c.cm.,	milk white } 40'—55' = 1 c.cm., milk white }	6.32
0.6			
		At 44' examined intestines. These were rather congested.	
		At 57' water let out of aortic balloon, which was redistended at 12.59.	
3.5	12.57—1.7 = 3.5 c.cm.,	whitish and bloody	6.23
		At 1.8 water let out of aortic balloon and portal ligature released.	
7	1.7—1.17 = 7 c.cm.,	very bloody, not so turbid	5.82
		At 17' aorta obstructed again.	
2.3	17'—40' = 5.4 c.cm.,	bloody	5.30
		(At 1.19 intestines cyanosed but not congested.)	
1.8	40'—50' = 1.8 c.cm.,	clear, bloody	4.9
		At 50' portal ligature tightened.	
1.6	50'—60' = 1.6 c.cm.		

It was pointed out by Emminghaus and confirmed by Cohnheim that the typical lymph of venous obstruction was more watery than normal lymph from the same part and at the same time contained red blood-corpuscles. Why then do we not observe a diminution in the solids of the lymph obtained from the liver, when the inferior vena cava is obstructed?

The composition of the lymph of venous obstruction is probably determined by two factors: the absolute rise of intracapillary pressure involved and the permeability of the capillaries in question. Thus after obstruction of the vena cava above the liver, the pressure in the hepatic capillaries, although much higher than normal, is probably not higher than the normal pressure in the intestinal capillaries; and it is possible that, if we were able to raise the pressure in the capillaries of the liver to the same extent as we do in the intestinal capillaries by ligature of

the portal vein, we should get from the liver an increased flow of more watery and bloody lymph. This idea is perhaps strengthened by the fact that one observes, after too rapid injection of blood into the right heart, an increased flow of lymph containing a large amount of red blood-corpuscles from the thoracic duct. On the death of the animal, haemorrhagic exudations may be found round the gall-bladder; the liver is intensely congested and the portal lymphatics filled with blood-stained lymph.

On the other hand, there is no doubt that the more permeable the capillary wall is, the greater range of pressure can it undergo, without any marked alteration in the composition of the transuded lymph. Very interesting in this respect are Jankowsky's experiments on the flow of lymph from the inflamed hind limbs of a dog. Of these I will here quote one or two¹.

"Exp. IX. July 13, 1882. Turpentine emulsion injected into both hind paws of a large dog.

July 14. Swelling of both paws. Lymph collected in the usual way. No pumping movements employed. Morphia injected. Left sciatic nerve divided. From the limb with intact sciatic 10 c.c. lymph were collected in 1 h. 18'. On the side with divided sciatic, the same amount was obtained in 50'. An elastic band was then tied round limb above the knee, without however obliterating the arterial pulse. After this, 10 c.c. of lymph were obtained on the paralysed side in 37', and on the other side, in 50'. The two latter portions of lymph were redder than the two first portions. All specimens of lymph clotted equally quickly.

Estimation of solids.

Inflammatory lymph from paralysed limb	5.745 %
" " " intact "	5.345 "
After obstruction of the veins:	
Inflammatory lymph from paralysed limb	5.975 "
" " " intact "	5.413 "
In another similar experiment, the solids were:	
Inflammatory lymph from paralysed limb	5.610 "
" " " intact "	4.775 "
After obstruction of the veins:	
Inflammatory lymph from paralysed limb	5.095 "
" " " intact "	4.743 "

We see then that an alteration of the permeability of the vessel

¹ Jankowsky. *Virchow's Archiv*, Vol. xciii. p. 259. 1883.

wall not only increases the amount of lymph produced by a given intracapillary pressure, but also increases the limits within which the pressure may be raised without causing a diminution in the proportion of solids in the lymph, so that a rise of pressure causes proportionately increased production of lymph of the same composition as that obtained under normal pressures.

Beyond pointing out this analogy between the hepatic capillaries and those of inflamed regions I am not inclined to go. Our knowledge of the properties of animal membranes and filtration through them is still too meagre to allow of our giving an exact account of the molecular changes involved in the changes of permeability of the vessel wall, and it would be profitless at this moment to indulge in speculation on the subject.

Changes in the blood caused by obstruction of the inferior cava above the diaphragm.

As might be expected, the increased transudation from the hepatic capillaries caused by obstruction of the inferior cava is not without effect on the general composition of the blood. Since the lymph is derived from the blood, we find after the obstruction that the percentage of solids in the whole blood is increased and this change is caused by a relative decrease in the amount of the blood plasma.

The changes in the blood serum are more interesting. Analyses of the blood serum (obtained from the femoral artery) have already been given in Experiment 4. Here it will be seen that the increased lymph-flow is attended by a diminution of solids in the serum. The serum from the femoral artery blood before the obstruction contained 7.33% solids. After the obstruction the solids in the serum fell to 7.02%, while the solids in the lymph had risen from 6.46% to 7.102%. We find here then exactly similar changes in blood and lymph as those produced by the injection of the various bodies included by Heidenhain in his first class of lymphagogues. Since in the latter case the lymph becomes more concentrated while the blood-plasma becomes less concentrated, Heidenhain concludes that a fluid more concentrated than the plasma has left the blood-vessels, and that there has therefore been an act of secretion on the part of the endothelial cells. If this argument were correct, we must regard Experiment 4 as a still more striking proof of secretory activity, since in this case the amount of solids in the lymph serum rose even higher than the amount in the serum of the corresponding sample of blood. There are two objections

however to this argument. In the first place if a fluid more concentrated than the plasma were secreted by the blood-vessels, one would expect the lymph from the thoracic duct to be also more concentrated than the blood plasma. This however is rarely or never the case after the injection of lymphagogues. In the second place Hamburger's results show that it is fallacious to conclude, because changes have taken place in the composition of the plasma, that these changes are necessarily conditioned directly by the composition of the exudation that has left the blood-vessels. They might in fact be caused by alterations in the relationship of the plasma to the corpuscles.

In the experiment of obstruction of the vena cava it is not sufficient to know the changes occurring in the blood from the femoral artery. We must also know how the blood is affected from which the exudation is taking or has taken place. For this purpose it is necessary to analyse samples of blood from the vena cava below the point of obstruction as well as the blood from the femoral artery. In the following experiment a large number of determinations of total solids were made in various samples of lymph-serum, blood and blood-serum. To obtain blood from the inferior cava the lower tube of the double obturator was made use of, blood being sucked up through this by means of a syringe. When it was desired to analyse the serum, the blood was received into small centrifuge glasses, which were at once corked, and after clotting, centrifuged. In this way, aeration being prevented, I hoped to obtain the original composition of the serum, whether from arterial or venous blood.

EXPERIMENT 16.

Simple obstruction of inferior cava above liver, with analyses of blood and lymph.

June 9, 1893. Large hairy dog about 13 or 14 kilos.

c.c. in 10 min.	Time	Lymph	Solids p.c.
6	11.50—12.0	= 6 c.cm., reddish yellow, rather cloudy.	
4.2	12.0—15'	= 6.2 c.cm., clear, light yellow	5.60
	At 12.5 blood-sample (1) about 20 c.cm.		
		Whole blood contained	22.29
		Blood-serum "	7.23
	Between 12.15 and 20' double obturator introduced.		
	Upper balloon distended in vena cava above liver, and lower opening left free for bleeding from lower part of vein.		

40	12.20—22 $\frac{1}{2}$ ' = 10 c.cm., reddish yellow	6.27
42	22 $\frac{1}{2}$ '—25' = 10.5 c.cm. „ „	
50	25'—27' = 10 c.cm.	6.76
33	27'—30' = 10 c.cm.	
33	30'—33' = 10 c.cm.	
36	33'—36' = 11 c.cm.	
	At 12.36 blood-sample (2) from lower (obstructed) part of vena cava.	
	Whole blood contained	26.57
	Serum „	7.67
	At 41' blood sample (3) from fem. art.	
	Whole blood contained	24.29
	Serum „	6.98
14	36'—42' = 11 c.cm. (not so red).	
11	42'—48' = 6.5 c.cm.	6.92
	Water let out of obturator at 12.48.	
20	48'—53' = 10 c.cm. (more opaque, whitish)	5.72
	Obturator removed at 12.54.	
13	12.53—1.0 = 9 c.cm.	
	At 12.55 blood sample (4) from fem. art. Serum contained	6.95
7	1.0—1.10 = 7 c.cm.	
5	10'—20' = 5 c.cm.	
4	20'—30' = 4 c.cm. (reddish)	5.56
	At 1.40 blood sample (5) from fem. art.	
	The serum contained	7.01
	At P.M. liver not congested. All specimens of lymph were clotted by 1.45.	

In this experiment the solids in the whole blood drawn from the femoral artery increased from 22.29% before the obstruction to 24.29% after the obstruction. In the blood-serum obtained at the same time the total solids diminished from 7.23% to 6.98%. At the same time that the latter specimen was drawn from the femoral artery a sample of blood was obtained from the vena cava below the obstruction. In this the increase of total solids was still larger, as it contained 26.57%. In the serum however a higher percentage of solids was obtained, viz. 7.67%, so that the idea is at once negatived that the capillary wall had secreted a lymph of higher concentration than the blood-plasma. How then are we to explain the increase in the total solids and the diminution in the solids of the serum of the systemic blood? It seems to me that in the case of obstruction of the cava, at any rate, the explanation is fairly simple.

It is well known that withdrawal of small quantities of blood from the circulation causes the specific gravity of the blood remaining in the body to be diminished in consequence of increased resorption of fluid from the tissues. Now after obstruction of the cava a large amount of blood is practically withdrawn from the circulation to fill the distended veins in the abdominal cavity. This causes a fall of systemic pressure, and therefore an increased resorption of lymph from the tissues. We have then the blood pouring out a concentrated lymph in the liver, and taking up a more dilute lymph from the tissues in the rest of the body, and the combination of these two processes must act in diminishing the total solids in the plasma or serum of the *circulating* blood.

Change in the coagulability of the lymph obtained after obstruction of the inferior cava.

Heidenhain pointed out that under these circumstances the coagulability of the lymph was much impaired, and in fact might be altogether lost. In my experiments I have also observed a distinct loss of coagulability, although this loss has never been complete (perhaps because I did not maintain the obstruction for a sufficient length of time). This impaired coagulability however is not a monopoly of the lymph. The blood drawn from the femoral artery after the obstruction of the inferior cava clots much more slowly and imperfectly than that obtained before the obstruction (cp. Exp. 4). If the blood be drawn from the inferior cava below the obstruction, the clotting is extremely slow, and the clot formed is soft and gelatinous. The slow clotting of venous blood is an oft-observed fact. In this case however the coagulability of the arterial blood is also affected. It would be a rash proceeding, in the present state of the coagulation question, to attempt to explain this delayed clotting of the blood. I merely wish to point out that in this respect the lymph follows the blood from which it has been derived—slowly coagulable blood giving rise to slowly coagulable lymph.

Hydraemic Plethora and Hydraemia.

Cohnheim pointed out that injection of large quantities of normal saline into the circulation so as to produce a hydraemic plethora caused a great increase in the amount of lymph flowing from the thoracic duct, so that this might be increased to 25 times the amount it was before. I give here the protocol of an experiment in which

hydraemic plethora was produced by the injection of 300 c.cm. warm normal saline. It will be seen that an enormous flow of lymph was produced, which was at its height immediately after the end of the injection and then gradually subsided. Three-quarters of an hour however after the injection the lymph-flow was still six times as fast as it had been previous to the injection. The stimulation of the splanchnics as well as the section of the two vagi was without effect on the course of the experiment.

EXPERIMENT 17.

Hydraemic Plethora.

Dog about 7 kilos. Both splanchnics divided and on electrodes. Renal vessels and ureters on both sides ligatured.

c.c. in 10 min.	Time	Lymph
2.6	12.40—55'	= 3.8 c.cm.
1.4	55'—1.5	= 1.4 c.cm.
2	1.5—1.15	= 2 c.cm.
(From 1.17 to 1.25, ran 300 c.cm. warm normal saline into jugular vein.)		
11	15'—25'	= 11 c.cm.
40	25'—35'	= 40 c.cm.
26	35'—38 $\frac{3}{4}$ '	= 10 c.cm. (excited splanchnics with strong currents).
18	38 $\frac{3}{4}$ '—44 $\frac{1}{4}$ '	= 10 c.cm. (rest).
16	44 $\frac{1}{4}$ '—50 $\frac{1}{2}$ '	= 10 c.cm. (rest).
22	50 $\frac{1}{2}$ '—55'	= 10 c.cm. (excited splanchnics).
Both vagi then cut.		
12.8	2.0—2.5	= 6.5 c.cm. (rest).
12.4	2.5—2.10	= 6.4 c.cm. (excited splanchnics).

As Bayliss and I have shown, hydraemic plethora is associated with a great rise of pressure in both portal vein and vena cava, so that there is a large rise of pressure in the capillaries of the intestines and liver. At the same time the chemical composition of the blood is altered. The question then arises as to which of these two factors is responsible for the enormous increase in lymph-flow observed under these circumstances.

Now, as we have shown in the preceding paper, we can eliminate the first factor altogether if we produce a simple hydraemia. If an equal volume of blood be withdrawn from the circulation before the injection of the normal saline fluid, there will be no rise of intra-

capillary pressure at all, whereas the composition of the blood will be altered in the same way as in hydraemic plethora.

It will be seen in the following experiment that the simple dilution of the blood has very little effect on the lymph-flow. Twice bleeding to 200 c.cm. and replacing the blood by normal saline, so that in all 400 c.cm. normal saline were injected, only increased the lymph-flow from 3.2 c.cm. to 5.2 c.cm. in 10 minutes, whereas in the last experiment, injection of 300 c.cm. normal saline increased the flow from 2 c.cm. in 10 minutes to 10 c.cm. in one minute. At the close of this experiment 350 c.cm. of normal saline were injected without previous bleeding, and the hydraemic plethora thus occasioned is attended with the usual consequences to the lymph-flow (cp. Exp. 8*, 13*, and 14* and Diagrams IX.* and X.*).

EXPERIMENT 18.

Hydraemia. Hydraemic Plethora.

Aug. 1, 1893. Dog about 8 kilos.

c.c. in 10 min.	Time	Lymph
3.3	2.10—30'	= 6.5 c.cm., opalescent, colourless.
3.2	30'—40'	= 3.2 c.cm., " "
		From 40' to 41', 200 c.cm. of blood withdrawn from femoral artery.
2.8	40'—50'	= 2.8 c.cm., getting slower towards end.
		From 50' to 53', injected 200 c.cm. warm normal saline (.75%) into jugular vein.
4.2	50'—60'	= 4.2 c.cm.
4.8	3.0—3.10	= 4.8 c.cm.
		From 3.10 to 3.11, withdrew 200 c.cm. of blood from femoral artery.
		From 3.11 to 3.14, injected 200 c.cm. of normal saline.
5.4	3.10—20'	= 5.4 c.cm.
5.4	20'—30'	= 5.2 c.cm.
		From 30' to 33', injected 330 c.cm. of normal saline.
20	30'—35'	= 10 c.cm.
37	35'—38'	= 11 c.cm.
33	38'—41'	= 10 c.cm.
18	41'—46½'	= 10 c.cm.
13	46½'—54'	= 10 c.cm.

It is evident then that the permeability, or sensitiveness to pressure, of the capillaries of the abdominal organs (especially the liver) is an important factor by which the blood may be rid of any increase in its bulk above normal. The part played by the hepatic capillaries in

getting rid of the excessive amount of fluid is illustrated by Johansson's and Tigerstedt's observations (*loc. cit.* in preceding paper).

Raum¹ too has pointed out that injection of normal saline into the blood gives rise to a vacuolation of the liver cells, so that part of the excess of lymph poured out by the hepatic capillaries is taken up by the cells of this organ, and indeed the increase in bulk of this organ caused by injection of large quantities of normal saline is in a large extent due to the dropsical swelling of the individual cells.

ON THE INFLUENCE OF NERVES ON LYMPH-SECRETION.

As I mentioned earlier, I began these investigations in the hope of finding some certain evidence of the existence of distinct lymph-secretory nerves. My experiments however have led me to the diametrically opposite conclusion, viz. that the nervous system has no direct influence on lymph-formation. Whenever in consequence of nerve-section or stimulation the lymph-flow is increased, the increase is always conditioned directly by an increased intracapillary pressure in the part, and therefore only indirectly by the nervous processes. The nervous system in fact can only influence the lymph-flow by altering the vascular conditions.

I will first describe my experiments, and try to show that in all of them the increase or diminution of lymph produced was directly due to a rise or fall of pressure in the capillaries of the abdominal organs.

Section of the cord in the lower cervical region.

As has been shown in the preceding paper, division of the cord causes a fall of pressure in the intestinal capillaries, while the pressure in the hepatic capillaries is probably unaffected or also falls slightly (cp. Exps. 10* and 11*).

In investigating the effect of division of the cord on the flow from the thoracic duct, a slight caution is necessary. The artificial respiration must be carried on at the same rate before and after division of the cord. If it be begun only after division of the cord, the increased movements of the abdomen may give rise to an apparent rise in the flow of lymph. If however this precaution be observed, section of the cord always produces a diminution in the flow from the thoracic duct, as shown in the following experiment.

¹ Raum. *Archiv f. exp. Path.* Vol. xxix. p. 353. 1892.

EXPERIMENT 19.

Division of cord at 7th cervical vertebra.

April 20, 1893. Small dog, about 6 kilos. Left vagus cut. Cannula in trachea. Dog in prone position.

Time	Lymph	Solids p.c.
11.30—40'	= 1.5 c.cm., colourless, opalescent.	
	Spinal cord exposed at 7th cervical vertebra. Artificial respiration set up.	
12.10—20'	= 2 c.cm.	4.48
	Spinal cord then divided.	
12.25—35'	= 0.75 c.cm.	4.73

The increase of solids observed in this experiment is not large enough to be of any great importance. We have here probably to do with a mixed lymph after as well as before the section. Here then the lymph-production is diminished *pari passu* with the pressure in the abdominal capillaries.

Influence of the splanchnic nerves.

Division of the splanchnics has no very great influence on the lymph-flow from the thoracic duct. In some of my experiments, the lymph-flow was temporarily increased. In others, as in the experiment here quoted, the amount of lymph obtained was practically unaltered. The composition of the lymph also underwent no change.

EXPERIMENT 20.

Division of splanchnics.

April 7, 1893. Dog about 8 kilos, very fat. Ligatures put loosely round both splanchnics from behind.

c.c. in 10 min.	Time	Lymph	Total solids in lymph p.c.
3	12.10—30'	= 6 c.cm., bloody, clots at once	5.74
2.75	30'—40'	= 2.75 c.cm.	5.62
	At 12.43 both splanchnics torn through.		
	The blood pressure fell to one-half but rose again in about 15 min.		
2	12.45—55'	= 2 c.cm. (clots continually in cannula)	5.70
2.1	55'—1.15	= 4.25 c.cm.	5.93
2.3	1.15—1.45	= 7 c.cm.	5.70

The effect of stimulation of the splanchnics on the flow of lymph was tried in one experiment by von Basch¹. This observer found that strong stimulation of the splanchnics for 10 seconds stopped the flow of lymph entirely. If, however, he had continued his stimulation for one or two minutes, he would have found that the preliminary stoppage or diminution of the flow gave way to an increase. If the splanchnic nerves be stimulated for many times in succession, it may be found that, in the later stimulations, there is no preliminary stoppage at all, the excitation of the splanchnic nerve causing at once an increase in the amount of lymph produced. The total effect of stimulation of the splanchnics is always an increase in the lymph flow. The increase, however, although constant, is not very large, amounting generally to about 50 % and never exceeding 100 %.

I give here protocols of two experiments, showing the effect of stimulation of the splanchnics on the flow and composition of the lymph. The composition of the lymph is practically unaltered, although in some cases, as in Exp. 24, a slight reddening of the lymph may be observed when these nerves are strongly stimulated.

EXPERIMENT 21.

Division of both splanchnics. Excitation of rt. splanchnic.

Saturday, July 9, 1892. Dog 6 kilos. Two splanchnics dissected. Ligature round left splanchnic. Rt. splanchnic divided and put on Ludwig electrodes.

Time	Lymph
11.10—20'	= 2.5 c.cm.
20'—30'	= 3 c.cm. (Excitation. R. A. 250—100. No effect on B. P.)
30'—40'	= 3.8 c.cm. (Excitation. R. A. 100—80.)
40'—50'	= 5.25 c.cm. (No excitation. At 11.45, left splanchnic torn through. A little blood in lymph.)
50'—12.0	= 3.5. (No excit.)
12.0—12.10	= 4.5 c.cm.
(12.0—12.2.	Excit. R. A. 65. Rise of pressure. Lymph stopped entirely.)
12.2—4'.	No excit. Lymph flows more quickly.
4'—5'.	Excit. Not a drop of lymph falls.
5'—10'.	No excit. First drop of lymph flows after 30 secs.)

¹ *Ludwig's Arbeiten*, 1875.

- 12.10—20' = 4.5 c.cm.
 (10'—14', excit. 14'—20', no excit.)
 20'—30' = 4 c.cm. (no excit.)
 30'—40' = 6.25 c.cm. (discontinuous excitation).
 (30'—31', excit. 31'—33', rest. 33'—34', excit. 34'—36', rest.
 36'—37', excit. 37'—40', rest.)
 40'—50' = 3.25 c.cm. (no excit.)
 50'—1.0 = 4.5 c.cm. (discontinuous excit. as from 30'—40').
 1.0—1.10 = 3.5 c.cm. (rest).
 10'—20' = 4.5 c.cm. (excite 1 min. in 3, as before).
 20'—30' = 3 c.cm. (rest).
 30'—40' = 2.75 c.cm. (rest).
 40'—50' = 4 c.cm. (excite three times for one minute).

EXPERIMENT 22.

Stimulation of both splanchnics.

April 22, 1893. Small dog about 5 or 6 kilos. Both splanchnics cut and provided with Ludwig electrodes, and arranged in circuit of the secondary coil of an Ewald inductorium.

Rate in 10 min.	Time	Lymph	Total solids in lymph p.c.
1.5	12.5—25' = 3 c.cm., opalescent, clots at once.		
	From 12.47 to 1.5 stimulated splanchnics. R. A. increased from 11 c.cm. to 7 c.cm. (an interval of 2 mins. in middle).		
1.5	12.45—1.5 = 3 c.cm. (excit.).		
2	1.5—1.15 = 2 c.cm. (rest).		5.7
	At 1.15, both vagi cut.		
1.75	15'—25' = 1.75 c.cm. (rest).		5.6
2.75	1.25—45' = 5.5 c.cm. (excite, R. A. 5).		5.1
3	45'—2.0 = 4.5 c.cm. (excited continuously).		
2	2.0—2.20 = 4 c.cm. (rest).		5.2
2.5	2.20—2.40 = 5 c.cm. (rest).		5.3
3	2.40—3.0 = 6 c.cm. (R. A. 4, excit.).		5.4
1.5	3.0—3.20 = 3 c.cm. (rest).		5.0

With each excitation of the splanchnics the lymph flowed quickly for the 1st minute and then gradually slowed off.

It has been shown in the previous paper that the pressure in the intestinal capillaries is increased after splanchnic excitation. During the excitation however although the pressure may also be slightly

increased, we cannot prove this with certainty, so that in this experiment an exact correspondence between lymph-production and capillary pressure, although probable, cannot be regarded as definitely ascertained (cp. Exp. 5* and Diagram II.*).

The effects on the flow of lymph of stimulating the vagus vary with the condition of the animal. In a normal animal excitation of the vagus may have very little effect or may cause a considerable increase in the lymph produced. The varying effect appears to depend on the length of time during which the heart's action can be entirely inhibited by the vagus. In many morphinised dogs it is difficult to produce a stoppage of more than 20 or 30 seconds by stimulation of the vagus. In such cases the lymph-flow is generally only slightly increased. If however the heart be stopped for 60 seconds or more, we may obtain a large increase of lymph-flow in consequence of the stimulation. This is well shown in the following experiment. During the early part of the experiment the vagus only stopped the heart for 20 to 30 seconds, and very little effect was produced on the lymph. Later on, after 20 minutes' rest (from 3.30 to 3.50), the first excitation of the vagus after the rest stopped the heart for 70 seconds, and at once a large increase of lymph-flow was observed. Then on repeated stimulation, the vagus once more failed to act so well and the increase of lymph-flow was only slight.

EXPERIMENT 23.

Dog about 8 kilos. Rt. vagus cut and on electrodes.

Time	Lymph
2.30—40'	= 2.8 c.cm.
40'—50'	= 3.2 c.cm. (from 40' to 45' stimulated vagus 4 times. Heart only stopped for a few seconds).
50'—60'	= 3.2 c.cm. At 50', left vagus cut.
3.0—3.10	= 3.2 c.cm. (exc. vagus at intervals. Heart only stopped 30 secs.).
3.10—20'	= 2 c.cm. (rest).
20'—30'	= 3.6 c.cm. (exc. vagus).
30'—40'	= 1 c.cm. (rest).
40'—50'	= 1.2 c.cm. (rest).
50'—60'	= 4.6 c.cm. (exc. vagus. In first 5 mins. vagus stopped heart for one minute. In last 5 mins. vagus standstill only lasted 30 secs.)
(50'—55')	= 3.2 c.cm.
55'—60'	= 1.4 c.cm.
4.0—4.5	= 0.6 c.cm. (rest).
4.5—10'	= 0.8 c.cm. (rest).

10'—15' = 3.3 c.cm. (exc. 10'—11'. Heart stopped 70 secs.
Exc. 12'—13'. Heart stopped 30 secs.)
15'—20' = 1.6 c.cm. (exc. 15'—16'. Heart stopped 40 secs.
Exc. 17'—18'. Heart stopped 30 secs.)
20'—30' = 1.2 c.cm. (rest).

Bayliss and I have shown that, on stoppage of the heart by the vagus, two phases may be distinguished in the venous pressures. (Cp. Exp. 3* and 10* and Diagrams V.* and VI.*) During the 1st period, which lasts for about 40 seconds after the commencement of stimulation, there is a slight fall in the portal pressure and a rise in the inferior cava pressure. After this time, the anaemia of the brain causes excitation of the vaso-motor centre and a rise of the general mean pressure, which is evidenced by a rapid rise of pressure in portal vein and vena cava. If then the stoppage of the heart only lasts for 20 to 30 seconds, we only get the 1st phase, i.e., a rise of pressure in the vena cava and a slight fall in the portal vein. Hence during long-continued stoppage of the heart, there is a much greater rise of pressure in the capillaries of the liver, and later on of the intestines, than when the stoppage is of only short duration. Coincident with this we find a greatly increased flow of lymph in the former condition, and only a slight increase in the latter.

If both splanchnics be cut at the commencement of the experiment, stimulation of the vagus has no influence on the lymph-flow, and may in fact cause a slight diminution. This is shown in the following experiment.

EXPERIMENT 24.

Splanchnics divided. Stimulation of splanchnics and vagus.
July 3, 1893. Dog. Both splanchnics on electrodes.

Time	Lymph
2.35—45' = 3.4 c.cm.	
From 45' to 50' left vagus cut and peripheral end arranged on electrodes.	
40'—60' = 3.2 c.cm.	
3.0—3.10 = 1.6 c.cm.	
10'—20' = 1.4 c.cm.	
20'—30' = 1.6 c.cm. (exc. left vagus with intermissions. Heart completely stopped during excitation).	
30'—40' = 1.4 c.cm. (rest).	
40'—50' = 2.2 c.cm. (at 50' rt. vagus cut), exc. vagus.	

3.50—4.5 = 2 c.cm. (rest).

4.5—4.20 = 4.4 c.cm. (exc. both splanchnics. R. A. 10. Lymph slightly reddened towards end).

4.10—35' = 5.4 c.cm. (rest).

35'—45' = 4.4 c.cm. (exc. splanchnics).

45'—60' = 4 c.cm.

4.0—4.10 = 3 c.cm. (vagus excited with intermissions. Heart stopped completely. R. A. 20).

10'—20' = 3 c.cm. (rest).

20'—30' = 3.4 c.cm. (exc. splanchnics. R. A. 10).

30'—40' = 2.2 c.cm. (rest).

40'—50' = 3.8 c.cm. (exc. splanchnics. R. A. 10).

With each stimulation of the splanchnics the lymph became slightly redder, and then recovered during the periods of rest.

Here again there is a complete correspondence between the effects of the vagus on the lymph and on the intracapillary pressure. As we have shown, stimulation of the vagus after section of the cord or of both splanchnics no longer causes the marked rise of venous pressure observed under normal conditions (cp. Exp. 1* and Diagram VII.*), and there is therefore no rise of capillary pressure in the abdominal organs under these circumstances.

In all these experiments then there is a complete agreement between the capillary pressures in the abdominal organs and the lymph-flow from the thoracic duct, and we must conclude that nerves have no influence on lymph-formation other than an indirect one through their effect on the circulation.

I believe that a consideration of previous work on the subject would lead one to the same conclusion. Although, as I have shown, the limb-vessels are ill adapted for investigations of this nature, we have the evidence of one observer, Rogowicz, to the effect that vascular dilation causes an increased production of lymph in the limbs. And this influence of vaso-motor section on lymph-production is still better shown in Jankowsky's experiments on inflamed limbs.

An experiment on which much stress has been laid is the oft-cited one of Ostroumoff. This observer showed that continued stimulation of one lingual nerve causes oedema of the same side of the tongue, which is described by Cohnheim as being very marked. I have repeated this experiment of Ostroumoff's five times, and cannot help thinking that there is either a good deal of enthusiasm in Cohnheim's description or else that Ostroumoff was dealing with hydraemic dogs.

For although in all my experiments I obtained a swelling of one side of the tongue on stimulation of one lingual nerve, the swelling was never so great as to deserve the term "ausgesprochenes Oedem." On cutting into the tongue at the end of the experiment the side on which the nerve had been stimulated was certainly moister than the other side, but the difference was extremely slight. That the lymph-flow in the tongue is increased coincidently with the vascular dilatation is shown by the experiments carried out by Rogowicz under Heidenhain's guidance. This increased flow is however sufficiently accounted for by the pronounced vascular dilation which is produced at the same time, and we have *no* right to assume that stimulation of the lingual nerve will produce an increased flow of lymph into the interstices of the tongue when the circulation through the tongue has ceased and there is no pressure in the capillaries of this organ.

In one experiment I observed a pronounced oedema of the tongue on stimulation of the lingual nerve. In this case however I had injected 600 c.cm. normal saline into the femoral vein, so that the dog was in a condition of hydraemic plethora. Before the saline was run in, the lingual nerve had been excited with gradually increasing stimuli for 40 minutes without the production of any oedema in the tongue. I would conclude then that there is no evidence of any direct action of nerves on the secretion or production of lymph.

We have thus come back to the point we started from. All my experiments on the lymph-flow from the thoracic duct under various conditions and the results obtained by Bayliss and myself on the venous pressures under similar conditions absolutely confirm Ludwig's views as to the formation of lymph, viz., that lymph-production is a function of the difference of pressure between the blood within the capillaries and the fluid in the tissue spaces outside them, and that, for any given area, increase of the intracapillary or decrease of the extracapillary pressure must determine an increased transudation, an increased lymph-formation. The normal permeability of a given capillary is no doubt intimately dependent on the life of the endothelial cells. Whether however any other process besides that of filtration is at work in the transudation of lymph through them, my experiments are not adequate to decide. I have, however, come across no facts which would negative the filtration hypothesis, and therefore cannot for the present regard as an article of faith Heidenhain's dictum that, normally, filtration plays no part in the formation of lymph,

“dass bei der Lymphbildung unter normalen Circulationsverhältnissen die Filtration keine Rolle spielt.”

I have, in conclusion, drawn up a tabulated list of the effects on the lymph-flow of the various experimental procedures employed. If this list be compared with the similar list at the conclusion of the paper on venous pressures, I think no one can fail to be persuaded that under normal conditions intracapillary pressure is the chief factor in lymph-production.

Procedure employed.	Effect on lymph-flow from thoracic duct.	Whether lymph is derived from intestines &c. or from liver.
Section of cord	Diminished	Probably both
Stimulation of vagus (splanchnics cut)	No effect or slight fall	?
Prolonged stimulation of vagus (normal)	Increased	?
Excitation of splanchnics	Increased	Probably both
Anaemia	Diminished	?
Hydraemic Plethora	Large increase	Both
Hydraemia	Slight increase	?
Obstruction of thoracic aorta	Diminished	Liver
Obstruction of inferior cava	Large increase	Liver
Obstruction of portal vein	Increased	Intestines &c.

Note. Hamburger has lately published an interesting paper on the lymph-flow from the main cervical lymphatic of the horse¹.

In this he comes to the conclusion that filtration can have nothing to do with the process of lymph-formation on the following grounds:

(1) That the amount of lymph produced may be increased under circumstances when the carotid pressure is diminished. It is perfectly well known that a single determination of arterial pressure is useless for judging of changes in intracapillary pressure, and without further observations, Hamburger's experiments neither confirm nor disprove the filtration theory.

(2) The proportional composition of blood-serum is not the same as that of the lymph produced at the same time.

(3) The osmotic pressure of the lymph is higher than that of the blood-plasma.

These two latter arguments lose a good deal of their weight if it be

¹ Hamburger. *Zeitschr. f. Biol.* Bd. xxx. p. 143. 1893.

remembered that the amount of lymph obtained is extremely small, and that we are perfectly ignorant what changes it has undergone on its way through the tissues from the blood-vessels to the cannula in the lymphatic duct. It is quite possible that the lymph may have taken up its excess of salts from the tissue cells, and that the fluid as it left the blood-vessels had the same or a lower osmotic pressure than the blood-plasma.

Since the final result of metabolism in the animal body or in an animal cell is disintegration, a breaking down of large complex unstable molecules of high potential energy into a great number of small simple stable molecules of small potential energy, the total output of an animal cell must have a higher osmotic pressure than the total income, so that all the metabolic changes in the tissues would tend to increase the osmotic pressure of the lymph with which they are bathed.

